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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,017	08/02/2001	Gregory S. Hamilton	AR762-XXA	7616

29728 7590 05/30/2003

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[REDACTED] EXAMINER

CHANG, CELIA C

[REDACTED] ART UNIT

PAPER NUMBER

1625

DATE MAILED: 05/30/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 09/920,017	Applicant(s) Hamilton et al.
Examiner Celia Chang	Art Unit 1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on Mar 12, 2003

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-3, 5-7, 9-11, and 13 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-3, 5-7, 9-11, and 13 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

4) Interview Summary (PTO-413) Paper No(s). _____

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____

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DETAILED ACTION

1. Amendment and response filed by applicants in Paper No. 17, dated mar. 18, 2003 have been entered and considered carefully. Claims 4, 8, 12, 14-82 have been canceled. Claims 1-3, 5-7, 9-11, 13 are pending.
2. Applicants' intention in removing the non-elected scope was incorrect since it has been clearly delineated that the current examination is limited to n=1 R2 is heterocycles of claim 3. Applicants provided no evidence that why the heterocyclic-pyrrolidinyl core is of the same core as pyrrolidinyl only core.
3. The rejection of claims 1, 2, 5, 6, 10 and 13 under 35 USC 112 second paragraph is maintained for reasons of record.

Claim 1 is ambiguous. It has been clearly delineated in the previous office action 'what' is examined for which the claim has not been limited to. In addition, the proviso conditions can only exclude anticipation but not obvious variations thereof such as homologs, one methyl addition compounds, isosteric replacements, position isomers etc. for which a tremendous amount of prior art existed and exhausted listing will not be made here but applicants are urged to consult the 26 pages of 1449 with all its references and compounds looking for homologs, one methyl addition compounds, isosteric replacements or position isomers which are well recognized *prima facie* structural obvious compounds over the provisoed compounds. One example is given here to illustrate the proviso (p.3 last para-p.4) that when D is bond, R2 is CONZ(R3) and R3 is formula on p.4 which is a isosteric replacement of compounds of US 6,291,510 col. 5 wherein the X2 is O or N, is replaced by its isosteric CH2 which is the instant claims. Due to the enormous amount of prior art both cited by the examiner and supplied on 26 pages of 1449 by applicants, individual rejections under 35 USC 103(a) for such structural homologs, one methyl insertions, isosteric replacements, position isomers etc. will not be listed.

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The rejection of claims 2 and 10 for R2 is "carbocyclic....selected from CH2..." is maintained for reason of record. Please note that the reference to claims 5 and 13 is only to point out the ambiguity wherein the scope of R2 can not be ascertained. If R2 is carbocyclic moiety made with CH2 then any aromatic ring system can not be within the scope yet the structural limitation of claim 3 indicated aromatic moieties. Applicants failed to delineate "what" is in and "what" is out, or "what" is R2, aliphatic cycles or aromatic cycles.

The rejection of claims 5 and 13 based on Ex parte Fressola is maintained for reasons of record. Please note that only n=1, R2 is heterocycle is the elected invention not all compounds of Tables I, II and III. Therefore, listing of compounds by name or structure such as found on pages 58-60 is proper and nothing impractical. Further, in so far particularly pointed our by name without referring to the specification.

The nomenclature of claim 6 does not read on compound 143. It is requested that IUPAC nomenclature be provided with structure for clarification.

4. The rejection of claims 1-2 and 9 under 35 USC 102(b) over Bycroft, Gold, Burbaum or Hamilton is dropped if the compounds highlighted in the previous office action fell within the proviso conditions. However, the generic teaching rendered the claims obvious since as it was explained supra the homologs, one methyl addition compounds, isosteric replacements, position isomers, which are structural prima facie would rendered the instant claims prima facie obvious and would not be repeated but incorporated by reference. The recommendation of deleting the non-elected subject matter and limiting the R2 to explicit structures of claim 3 is still made.

5. The rejection of claims 1-3, 5, 8-11 under 35 USC 102(f) over WO 99/14998 is maintained for reason of record.

Please note that both SN 60/059,905 and 60/059,963 are filed in 1997. The earliest filing date based on the CIP date of SN 09/204,237 is 1998. Therefore, the 102(f) issue is correct.

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Applicants must provide evidence as to "who" is the first to invention since all the compounds of the claims are owned and used by Magal before the instant application was filed.

6. The rejection of claims 1, 2, 6-7, 9-10 under 35 USC 102(e), (f) or (g) over Brumby, Kato supplemented by Anderson is maintained for reasons of record.

Applicants argued that the instant provisional filing date preceded Brumby and Kato, therefore, traverse the rejection. Please note that while the generic term carboxylic isostere encompassing the species of Brumby or Kato was filed in the provisional 60/087,788, no species corresponding to the species as explicitly disclosed by Brumby or Kato was filed or find descriptive support in the provisional filing (in re Baird 29 USPQ2d 1550). Therefore, in so far as the species is concerned, applicants are not entitled to the Jun 3, 1998 filing date of 60/087,788 since addition of Brumby or Kato species of the isostere would be "new matter". Yet, the species of Brumby or Kato **anticipates** the genus, i.e. claim 1-2, 6-10. Therefore, in so far as claims 1, 2, 6-10 is concern, the rejection is proper. Applicants' argument of priority benefit can only be applicable to claim 3 wherein explicit R2, demarcated from Brumby or Kato is limited.

7. The rejection of claims 1-3, 9-11 under 35 USC 103(a) over US 5,859,031, 5,945,441, 6,177,455 or 6,291,510 in view of Silverman or Bungaard further in view of US 5,801,187 and 6,218,544 is maintained for reason of record.

Applicants argued that the primary references are subject to an obligation to assignment to GPI NIL Holdings, Inc., thus, co-owned at the time the invention was made, therefore, qualifies for 103© not 103(a). This is erroneous. Please note that the instant application has a "different" inventive entity from all four primary references. Further, the instant application, at the time the invention was made, was assigned to GPI HIL Holdings, Inc. and Amgen, INC. (See assignment for 60087788 attached) therefore, does not have the "same" person as assignee. The 103(a) rejection is proper.

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8. The rejection of claims 1-3, 9-11 under judicially created doctrine of obviousness-type double patenting over US 5,859,031, 6,291,510 in view of Silverman or Bungaard further in view of Li 5,801,187 or 6,218,544 is maintained for reason of record.

Applicants argued that is that there must be "some suggestion" and some "reasonable expectation" in establishing a case of *prima facie* obviousness that an ester is a prodrug of free carboxylic acid compound.

Please note that, the Silverman or Bungaard references disclosed that esters will be hydrolyzed *in vivo* because of the abundant existence of liver, blood or organ esterase. Therefore, esters *will be hydrolyzed in vivo* is factual not mere suggestion. Since hydrolysis is factual, it will happen, the free acids will exist *in vivo*. Applicants then presented a self conflicting argument by alleging unpredictability of the activity of the free acid. The question of whether hydrolyzed ester i.e. free acid, will have activity is unpredictable will face conflicting issues. If applicants are alleging that the free acid does "not" having activity, then, the instant claims must face a 101 or 112 first paragraph issue. The examiner, however, received the claim on its face as disclosed by applicants that the acid is active. Then, for applicants to receive independent and distinct patent of the free acids under "unexpected results", applicants need to demonstrate that the ester of the prior art "having activity of its own" not depending on the hydrolyzed acid for activity or the hydrolysis does not hydrolyze rapid enough to give sufficient free acid thus the ester is not a good prodrug for the acid. Please note that without explicit demonstration, whether an ester upon administration is active in its intact ester or is active after hydrolysis can not be distinguished. While the examiner provided teaching of the art to indicated reasonable expectation of an ester being hydrolyzed *in vivo*, thus, rendered the acid *prima facie* obvious, a rebuttal of applicants of "unexpected" result of not rapid enough must be supported by factual evidence.

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9. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 703-308-4702. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman, can be reached on (703) 308-4698. The fax phone number for the organization where this application or proceeding is assigned is 703-308-7922.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

WP/Chang
May 28, 2003


Celia Chang
Primary Examiner
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